



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: Box ISSUE FEE
COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

18M2/0419

STACEY R. SIAS, PH.D.
HOFFMAN-LA ROCHE INC.
340 KINGSLAND STREET
NUTLEY, NJ 07110

NOTICE OF ALLOWANCE
AND ISSUE FEE DUE

- ☐ Note attached communication from the Examiner
☐ This notice is issued in view of applicant's communication filed

1814 04/19/94

SERIES CODE/SERIAL NO. 077695-201	FILING DATE 02/91	TOTAL CLAIMS 021	EXAMINER AND GROUP ART UNIT PROUTY, R	DATE MAILED
RUSSELL G.				
HIGUCHI,				
HOMOGENEOUS METHODS FOR NUCLEIC ACID AMPLIFICATION AND DETECTION				

TITLE OF
INVENTION

ATTY'S DOCKET NO. 1 2599	CLASS-SUBCLASS 435-006-000	BATCH NO.	APPLN. TYPE A12 UTILITY	SMALL ENTITY NO	FEE DUE \$1170.00	DATE DUE 07/19/94
-----------------------------	-------------------------------	-----------	----------------------------	--------------------	----------------------	----------------------

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT.
PROSECUTION ON THE MERITS IS CLOSED.**

**THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS
APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.**

HOW TO RESPOND TO THIS NOTICE:

I. Review the SMALL ENTITY Status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

- A. If the Status is changed, pay twice the amount of the FEE DUE shown above and notify the Patent and Trademark Office of the change in status, or
B. If the Status is the same, pay the FEE DUE shown above.

If the SMALL ENTITY is shown as NO:

- A. Pay FEE DUE shown above, or
B. File verified statement of Small Entity Status before, or with, payment of 1/2 the FEE DUE shown above.

II. Part B of this notice should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by a charge to deposit account, Part B should be completed and returned. If you are charging the ISSUE FEE to your deposit account, Part C of this notice should also be completed and returned.

III. All communications regarding this application must give series code (or filing date), serial number and batch number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees.

PATENT AND TRADEMARK OFFICE COPY



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
07/695,201	05/02/91	HIGUCHI	R 2599

STACEY R. SIAS, PH.D.
HOFFMAN-LA ROCHE INC.
340 KINGSLAND STREET
NUTLEY, NJ 07110

18M2/0419

PROUTY, FRAMINER

ART UNIT PAPER NUMBER

1814

04/18/94

DATE MAILED

NOTICE OF ALLOWABILITY

PART I

- ☒ This communication is responsive to request for record, filed 1/14/94
- ☒ All the claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice Of Allowance And Issue Fee Due or other appropriate communication will be sent in due course.
- ☒ The allowed claims are 1, 2 and 4-22
- ☐ The drawings filed on _____ are acceptable.
- ☐ Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has [] been received, [] not been received, [] been filed in parent application Serial No. _____, filed on _____.
- ☒ Note the attached Examiner's Amendment.
- ☒ Note the attached Examiner Interview Summary Record, PTOL-413.
- ☒ Note the attached Examiner's Statement of Reasons for Allowance.
- ☐ Note the attached NOTICE OF REFERENCES CITED, PTO-892.
- ☒ Note the attached INFORMATION DISCLOSURE CITATION, PTO-1449.

PART II

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" indicated on this form. Failure to timely comply will result in the ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

- ☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.
- ☒ APPLICANT MUST MAKE THE DRAWING CHANGES INDICATED BELOW IN THE MANNER SET FORTH ON THE REVERSE SIDE OF THIS PAPER.
 - ☒ Drawing informalities are indicated on the NOTICE RE PATENT DRAWINGS, PTO-948, attached ~~hereto~~ to Paper No. 10. CORRECTION IS REQUIRED.
 - ☐ The proposed drawing correction filed on _____ has been approved by the examiner. CORRECTION IS REQUIRED.
 - ☐ Approved drawing corrections are described by the examiner in the attached EXAMINER'S AMENDMENT. CORRECTION IS REQUIRED.
 - ☒ Formal drawings are now REQUIRED.

Any response to this letter should include in the upper right hand corner, the following information from the NOTICE OF ALLOWANCE AND ISSUE FEE DUE: ISSUE BATCH NUMBER, DATE OF THE NOTICE OF ALLOWANCE, AND SERIAL NUMBER.

Attachments:

- ☒ Examiner's Amendment
- ☒ Examiner Interview Summary Record, PTOL-413
- ☒ Reasons for Allowance
- ☒ Notice of References Cited, PTO-892
- ☒ Information Disclosure Citation, PTO-1449

- ☐ Notice of Informal Application, PTO-152
- ☐ Notice re Patent Drawings, PTO-948
- ☐ Listing of Bonded Draftsmen
- ☐ Other


ROBERT A. WAX
SUPERVISORY PATENT EXAMINER
GROUP 180

Serial Number: 07/695,201

-2-

Art Unit: 1814

1. An Examiner's Amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. § 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the Issue Fee.

Authorization for this Examiner's Amendment was given in a telephone interview with Ken Weber on 4/13/94.

EXAMINER'S AMENDMENT

In Claim 1, line 8, delete --distinguishable from the-- and replace with --greater than the amount of said--.

Cancel Claim 3.

In Claim 11, line 6, delete --PCR-- and replace with --a polymerase chain reaction (PCR)--.

In Claim 11, lines 9-10, delete --distinguishable from the-- and replace with --greater than the amount of said--.

In Claim 14, line 2, insert --the-- following
--throughout--.

In Claim 17, line 2, insert --wherein said intercalating agent is characterized as providing a detectable signal when bound to double stranded DNA, which signal is greater than the signal provided by said intercalating agent when it is unbound--
following --intercalating agent--.

C1

45

Art Unit: 1814

2. The following is an Examiner's Statement of Reasons for Allowance:

The declarations and third party statement submitted by applicants are convincing to show that one of ordinary skill in the art would not have been motivated by to add ethidium bromide (EtBr) to a polymerase chain reaction because the EtBr/DNA ratios taught by the invention are reported by Kaledin et al. to be at least 50% inhibitory to polymerization activity from a double stranded DNA template. Furthermore, the declarations convincingly show that one of ordinary skill in the art would not rely on the teachings of Kaledin et al. because the effects of EtBr on a PCR reaction in which the large majority of DNA present is single stranded might be radically different than the effects seen by Kaledin et al. in a reaction in which most of the DNA was double stranded. The declarations and third party statement provide evidence that one of ordinary skill in the art would reasonably expect a PCR reaction to be especially inhibited by intercalating agent such as EtBr because PCR requires complete extension and duplex denaturation while the assays taught by both Kaledin et al. and Sutherland et al. both do not.

Any comments considered necessary by applicant must be submitted no later than the payment of the Issue Fee and, to avoid processing delays, should preferably accompany the Issue Fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

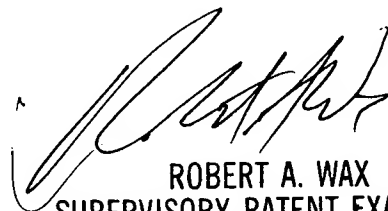
Serial Number: 07/695,201

-4-

Art Unit: 1814

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D., whose telephone number is (703) 308-4000.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

A handwritten signature in black ink, appearing to read 'R. Wax', is positioned above the printed name and title.

ROBERT A. WAX
SUPERVISORY PATENT EXAMINER
GROUP 180